

AMENDMENTS

In the Specification:

At page 5, please insert the following replacement paragraph.

[0018] Further embodiments include methods of treating a disease associated with neo-vascularization comprising administering a peptide that selectively binds aminopeptidase A. The peptide may inhibit aminopeptidase A. The peptide may be selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3. The subject may be a mammal and is typically a human. The peptide is administered in a pharmaceutically acceptable carrier. The method may further comprise administering a second therapeutic agent to said human. The peptide may be operatively coupled and in particular covalently coupled to a therapeutic agent. A therapeutic agent may be a drug, a chemotherapeutic agent, a radioisotope, a pro-apoptosis agent, an anti-angiogenic agent, a hormone, a cytokine, a cytotoxic agent, a cytotoxic agent, a cytostatic agent, a peptide, a protein, an antibiotic, an antibody, a Fab fragment of an antibody, a hormone antagonist, a nucleic acid or an antigen. The anti-angiogenic agent is selected from the group consisting of thrombospondin, angiostatin5, pigment epithelium-derived factor, angiotensin, laminin peptides, fibronectin peptides, plasminogen activator inhibitors, tissue metalloproteinase inhibitors, interferons, interleukin 12, platelet factor 4, IP-10, Gro- β , thrombospondin, 2-methoxyoestradiol, proliferin-related protein, carboxyamidotriazole, CM101, Marimastat, pentosan polysulphate, angiopoietin 2 (Regeneron), interferon-alpha, herbimycin A, PNU145156E, 16K prolactin fragment, Linomide, thalidomide, pentoxifylline, genistein, TNP-470, endostatin, paclitaxel, Docetaxel, polyamines, a proteasome inhibitor, a kinase inhibitor, a signaling peptide, accutin, cidofovir, vincristine, bleomycin, AGM-1470, platelet factor 4 and minocycline. Whereas, the pro-apoptosis agent is selected from the group consisting of etoposide, ceramide sphingomyelin, Bax, Bid, Bik, Bad, caspase-3, caspase-8, caspase-9, fas, fas ligand, fadd, fap-1, tradd, faf, rip, reaper, apoptin, interleukin-2 converting enzyme or annexin V. Additional apoptotic agents include gramicidin, magainin, mellitin, defensin, cecropin, (KLAKLAK)₂ (SEQ ID NO:15), (KLAKKLA)₂ (SEQ ID NO:16), (KAAKKAA)₂ (SEQ ID NO:17) or (KLGKKLG)₃ (SEQ ID NO:18). Furthermore, a cytokine may be selected from the group consisting of interleukin 1 (IL-1), IL-2, IL-5, IL-10, IL-11, IL-12, IL-18, interferon- γ (IF-

γ), IF- α , IF- β , tumor necrosis factor- α (TNF- α), or GM-CSF (granulocyte macrophage colony stimulating factor).

Please delete the Sequence Listing numbered pages 1 through 4 and insert therefor the Substitute Sequence Listing numbered pages 1 through 5 as submitted electronically herewith as text.

At page 21, paragraph [0054], please insert the following replacement paragraph:

[0054] Briefly, 10^{10} transducing units (TU) of a CX₃CX₃CX₃C (SEQ ID NO:14; C, cysteine; X, any amino acid residue) phage display random library are pre-absorbed on SK-RC-49 parental cells. The pre-cleared CX₃CX₃CX₃C phage library ($\sim 10^{10}$ TU) is added to 106 detached APA-transfected SK-RC-49 cells in binding medium (20 mM HEPES, 2% FCS in DMEM). Cell panning was performed at 4° C. to minimize post-binding events such as receptor-mediated internalization (Giordano et al., 2001). Cells were washed with binding medium and cell bound phage were recovered and amplified by infection of K91Kan E. coli. Serial dilutions were plated on Luria-Bertani (LB) agar plates with tetracycline and kanamycin. The number of TU was determined by bacterial colony counting.

At page 22, paragraph [0056], please insert the following replacement paragraph:

[0056] Phage libraries displaying linear, cyclic, or double cyclic peptides may be used within the scope of the present invention. However, phage libraries displaying 3 to 10 random residues in a cyclic insert (CX₃-10C) are preferred, since single cyclic peptides tend to have a higher affinity for the target organ than linear peptides. Libraries displaying double-cyclic peptides (such as CX₃CX₃CX₃C; SEQ ID NO:014; Rojotte et al., 1998) may also be used. However, the production of the cognate synthetic peptides, although possible, can be complex due to the multiple conformers with different disulfide bridge arrangements. APA targeting peptides typically will bind APA, subsequent to binding the APA and targeting moiety are internalized by endocytosis.

At page 28, paragraph [0079], please insert the following replacement paragraph:

[0079] Proteins or peptides may be made by any technique known to those of skill in the art, including the expression of proteins, polypeptides or peptides through standard molecular biological techniques, the isolation of proteins or peptides from natural sources, or the chemical synthesis of proteins or peptides. The nucleotide and protein, polypeptide and peptide sequences corresponding to various genes have been previously disclosed, and may be found at computerized databases known to those of ordinary skill in the art. One such database is the National Center for Biotechnology Information's Genbank and GenPept databases (www.ncbi.nlm.nih.gov) ([world wide web at ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)). The coding regions for known genes may be amplified and/or expressed using the techniques disclosed herein or as would be known to those of ordinary skill in the art. Alternatively, various commercial preparations of proteins, polypeptides and peptides are known to those of skill in the art.

At page 54, paragraph [0167], please insert the following replacement paragraph:

[0167] A variety of crystal structures are available in the Protein Data Bank (www.rcsb.org/pdb/) ([world wide web at rcsb.org/pdb/](http://www.rcsb.org/pdb/)). These structures may be used as model structures to identify sites on the proteins that could be targeted by small molecule chemical inhibiting compounds.